

**We claim:**

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1. A method for targeting degradation of a polypeptide in vivo comprising:  
providing a ubiquitin protein ligase polypeptide that encodes a ubiquitin conjugation activity, which is functionally linked to a target polypeptide interaction domain that provides a target polypeptide recruitment activity;  
expressing said ubiquitin protein ligase polypeptide-target polypeptide interaction domain hybrid in a cell;  
recruiting the target polypeptide to said ubiquitin protein ligase polypeptide; and  
ubiquitinating the target polypeptide,  
thereby forming a ubiquitin-target polypeptide conjugate which is targeted for degradation.
2. The method of claim 1, wherein the ubiquitin-target polypeptide conjugate further undergoes ubiquitin-dependent proteolysis.
3. The method of claim 2, wherein said ubiquitin-dependent proteolysis is by the proteasome.
4. The method of claim 1 wherein the ubiquitin protein ligase polypeptide is an E3 ubiquitin protein ligase.
5. The method of claim 4, wherein the E3 ubiquitin protein ligase is selected from the group consisting of: an SCF polypeptide, a HECT polypeptide, and a UBR1 polypeptide.
6. The method of claim 5, wherein the SCF polypeptide is an F-box polypeptide.
7. The method of claim 6, wherein the F-box polypeptide further comprises a WD domain.
8. The method of claim 6, wherein the F-box polypeptide is selected from the group consisting of Cdc4p, Pop1p, Pop 2p, Grr1p, Met30p, HOSp, beta TrCPp, and FWD1p.
9. The method of claim 6, wherein the F-box polypeptide is a polypeptide selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, and 12.
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10. The method of claim 6, wherein the F-box polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID Nos. 1, 3, 5, 7, 9, and 11.

11. The method of claim 5, wherein the SCF polypeptide is selected from the group consisting of: a Cdc4 polypeptide, a Skp1 polypeptide or a cullin polypeptide.

12. The method of claim 5, wherein the HECT polypeptide is selected from the group consisting of E6-AP, Nedd-4, RSP5, Smurf1, TOM1 and EDD.

13. The method of claim 5, wherein the E3 ubiquitin protein ligase is a yeast or a mammalian UBR1 polypeptide.

14. The method of claim 1, wherein the target polypeptide interaction domain is selected from the group consisting of a papillomavirus E7 polypeptide, and an SV40 LTP polypeptide.

15. The method of claim 1, wherein the target polypeptide is selected from the group consisting of a retinoblastoma polypeptide, a p107 polypeptide, IκB, Sic1p, Cln2p, E2 or beta-catenin.

✓ 16. A method for decreasing the level of a target polypeptide comprising:  
providing an SCF recruitment domain which is operably linked to a target polypeptide interaction domain to form an SCF recruitment domain-target polypeptide interaction domain fusion protein; and  
expressing the SCF recruitment domain-target polypeptide interaction domain fusion protein such that the level of said target polypeptide is decreased.

17. The method of claim 16, wherein the SCF recruitment domain is an F-box polypeptide.

18. The method of claim 17, wherein the F-box polypeptide further comprises a WD domain.

19. The method of claim 17, wherein the F-box polypeptide is selected from the group consisting of Cdc4p, Grr1p, Pop1p, Pop 2p Met30p, HOSp, betaTrCp, and FWD1.

20. The method of claim 14, wherein the F-box polypeptide is at least 70% to a polypeptide of at least 20 contiguous amino acids of a polypeptide selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10, and 12.

21. The method of claim 17, wherein the F-box polypeptide is encoded by a nucleic acid which hybridizes to a nucleic acid selected from the group consisting of 1, 3, 5, 7, 9, and 11.

22. A method for creating a destabilized polypeptide subject to SCF-mediated proteolysis comprising:  
providing an SCF recruitment domain; and  
operably linking the SCF recruitment domain to the polypeptide, thereby creating the destabilized polypeptide subject to SCF-mediated proteolysis.

23. A method for expressing a destabilized target polypeptide subject to SCF-mediated proteolysis comprising:  
providing an SCF recruitment domain which is operably linked to a target polypeptide and expressing the SCF-target polypeptide fusion, thereby expressing a destabilized target protein.

24. A nucleic acid for expressing an SCF recruitment domain- target polypeptide interaction domain comprising:  
a nucleic acid encoding an SCF recruitment domain; and  
a nucleic acid encoding a heterologous polypeptide domain;  
wherein the nucleic acid encoding the SCF recruitment domain and the nucleic acid encoding the heterologous polypeptide domain are operably linked so as to encode an SCF recruitment domain-heterologous polypeptide domain fusion protein.

25. The nucleic acid of claim 24, wherein the heterologous polypeptide domain is a target polypeptide.

26. The nucleic acid of claim 24, wherein the heterologous polypeptide domain is a target polypeptide interaction domain.

27. The nucleic acid of claim 24, wherein the nucleic acid encoding the SCF recruitment domain is at least 90% identical to a nucleic acid selected from the group consisting of SEQ ID Nos. 1, 3, 5, 7, 9, and 11.

28. The nucleic acid of claim 24, wherein the nucleic acid encoding the SCF recruitment domain hybridizes under stringent conditions to nucleic acid selected from the group consisting of SEQ ID Nos. 1, 3, 5, 7, 9, and 11.

29. A vector comprising a nucleic acid encoding an SCF recruitment domain and a cloning site for inserting an heterologous polypeptide encoding sequence.

30. A vector comprising a nucleic acid of claim 24.

31. A cell comprising a vector of claim 29 or claim 30.

32. A method of treating a cell to stabilize a target polypeptide of ubiquitin protein ligase comprising contacting the cell with a preparation comprising an effective amount of an organic compound which can competitively inhibit interaction of the target polypeptide with the ubiquitin protein ligase.

33. The method of claim 32, wherein the organic compound is a peptide or peptidomimetic.

34. The method of claim 33, wherein the peptide or peptidomimetic is a competitive inhibitor of a WD domain.

35. The method of claim 33, wherein the peptide or peptidomimetic comprises a general chemical formula of  $G-H-X^{(3-6)}-h-X-X-h-X-r-X-t^{(2-3)}-p-X-h-h-X-X-X-X-D-X-X-X-X-h-W-D$ .

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E2(E39A) over time were determined by immunoprecipitation followed by immunoblotting using the anti-EE monoclonal antibody (Babco).

To demonstrate the efficacy of the engineered ubiquitin system in mammalian cells, the human osteosarcoma Saos-2 cells lacking endogenous pRb were co-transfected with 5ug each of HA-tagged pRB and F-TrCP-E7(N) (lanes 1-3), or with 5ug each of HA-pRB and F-TrCP-E7(N)(ΔDLYC) (lanes 4-6) using the FuGENE transfection reagent, respectively. 36 hours after transfection, cells were starved for 1 hour in DMEM media without L-Met and L-Cys, pulse labeled for 1 hour with the <sup>35</sup>S-Express labeling mix, and then chased with fresh DMEM media containing 15% fetal calf serum at times 0, 3 hours and 6 hours. Cell lysates were prepared in NP-40 lysis buffer and 200 ug of each extracts were subjected to immunoprecipitation by the 12CA5 monoclonal antibody.

## 6. Polypeptide and Nucleic Acid Compositions

### F-Box Polypeptides and F-Box Encoding Nucleic Acids

The F-box protein Cdc4p is encoded by a nucleic acid sequence corresponding to nucleotides 7558 to 9897 of GenBank Accession No.D31600 (SEQ ID No. 1) as shown below, and which encodes the F-box protein corresponding to GenBank Accession No. BAA06495 (SEQ ID No. 2) as shown below.

#### SEQ ID No. 1

1 ggatccgtgt cgtaactgcg ttccgtacac cttaaaatga actttccagc aggtgcacca  
61 ttttccaatc cattgaaaaa tcttactgat tcttcgacct cctcctgggt taagtgtgtc  
121 tccaaatgaa tatatagcag ccaaataat atgtttgatc taccctttgg ctctgtatttc  
181 gaatagtcca gtatatcaaa taatgttggt gcataagctg cttttgatcc ttgtttttca  
241 ttttccgctt ccgtttcttt tacttcattc tgttcattca ccatatcttg ctctgagct  
301 ttcgatttga cttccacata cttggaaaga aacctcttgt caattaggcc ggaattatca  
361 catatgctaa acaacatatt aataatgtta aatttggtta cgggtgtccac ttcaccatca  
421 ttttggttga ctttttttga agtctccatc aatgagagtt gctcattgcc ccacggcaga  
481 tttttcagaa tagatttcag tctaggtgta tcttgcaaaa gtttcggatc attggcatgt  
541 aattgtaaaa ctggcacgga gtgaaaagtt ctcaattgag atgtcatttc taaataaaaa  
601 tttatagtgg tgttcaacct accaatgttg accaataacg ctaaaacaca agtagaaaat  
661 gctacttggt ggtctcaataa tagtttatct ctgagaattt tggaaacatt gatagaagtg  
721 gctattgtca acacatataa ttgtgcgaac gtcaatttat cgttaaatac aaatgtcctt  
781 gcacgtact ctttgtcgtt cacgttgatt gataatttat cgccatcgat attaattgggt  
841 acaatagagt tcttgtatag gggttttaga acattagtga agatttgcct cttgtccatc  
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Cont

961 ttcttcaaat gagattgta ttactggca ttgctttctt tgggttctct tctaacagtg  
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1081 tcgaagttga gcaagatgtt ggtattttct tcttcacttt gcgtggagtc atcatcattt  
1141 ttatcgtcga tttaaatctc gtgtataact ggaatgcttt ttgtagtcac agtctcggtc  
1201 tctgattgaa tggagcttgg ggatgcttct tcttgatgc ccgattttac agattgcatt  
1261 ggagaatctg cttttgttcc gtcagaattg tcttctcgta gttggaaagt atcatgaatt  
1321 ggatcgata ctctcttccc catctttaat tagagtgtcg cttttattta gctttcgatt  
1381 ttacttagtt aatcatgaac tgtttccaat accatatcag cattcattgg gcgttcttta  
1441 cttacttgta ccgttaacgc attcgagggt aacctgtttt tcgttgtaaca cgatatgcta  
1501 cagaattgtc ttaatatggg ctaagaaaaa aaaaagtctg attatttctg atactgcaaa  
1561 atatatactg gcttggttaa gaaaagtgtt gcttttagttc ctttacatca agagtcgtta  
1621 aattgttttg tgtcataaca gtagtggctt tttgagacat caatcgactc tcagggtttc  
1681 cttctgttca tcttcttgtt ttcggtaaag gtcagccagc atatttcaat tctctctttt  
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1921 cagtttaaaa aaatatgtac gtgtataata actgaattta aaaggatagt aaataatttt  
1981 tgcattttat ggaatgtcaa aataactaata agtcgcaaat atagctatca aataccataa  
2041 tttagctact tatagaaaga tgcccaaatc ccgacaaaaa aggaccattg cgtcttctc  
2101 gtcagttttt tatggaagtt cacctttcca aaatgatggc tacatcaaag taatggaact  
2161 cgtatcacac attgtcattg aaataaatca ttcacctacc gcaacaacgg atgaaacgag  
2221 aaagcagaat aatccggagc tgaaagtga agaaccagtt tgtaacctca agaagtggga  
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2341 agataggata cgtaagtggg ttagaagaca tatattaaag gaagagatcg aaatcctttc  
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cont

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3481 actcagttga ctgattatga aagatatggc gtagccgttg ggtaggggtt attacacaga  
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3601 aaggaattgt tatataagga cacaagaaat gtgttggtac gctctgcgcc tcaatgacgg  
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The human F-box protein h $\beta$ TrCp is encoded by a nucleic acid sequence corresponding to GenBank Accession No. NM\_003939 (SEQ ID No. 3) as shown below, and which encodes the F-box protein corresponding to GenBank Accession No. 4502477 (SEQ ID No. 4) as shown below.

## SEQ ID No. 3

1 tgcgttggtc gcggcctggc accaaagggg cggccccggc ggagagcggg cccagtggcc  
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1441 gaatgtggtg catgtttacg agtgtagtaa ggccatgagg aattggtgcg ttgtattcga  
1501 tttgataaca agaggatagt cagtggggcc tatgatggaa aaattaaagt gtgggatcct  
1561 gtggctgctt tggatccccg tgctcctgca gggacactct gtctacggac ccttgtggag  
1621 cattccggaa gagtttttcg actacagttt gatgaattcc agattgtcag tagttcacat  
1681 gatgacacaa tctcatctg ggacttccta aatgatccag ctgccaagc tgaaccccc  
1741 cgttccccct ctcgaacata cacctacatc tccagataaa taaccatata ctgacctcat  
1801 acttgcccag gaccatttaa agttgcccga tttacgatat ctgccaatac caggatgagc  
1861 aacaacagta acaatcaaac tactgccag tttccctgga ctagccgagg agcagggtct  
1921 tgagactcct gttgggacac agttggtctg cagtcggccc aggacggtct actcagcaca  
1981 actgactgct tcagtgtgct tatcagaaga tgtcttctat caattgtgaa tgattggaac  
2041 ttttaaactt cccctcctct cctcctttca cctctgcacc tagttttttc ccattggttc  
2101 cagacaaagg tgacttataa atatatttag tgttttgcca gaaaaaaaaa a

#### SEQ ID No. 4

1 mdpaeavlqe kalkfmnsse redcnngesp rkiipekns1 rqtynscarl clnqetvcla  
61 stamktencv aktklangts smivpkqrkl sasyekel cvkyfeqwse sdqvefvehl  
121 isqmchyghg hinsylkpm1 qrdftalpa rgldhiaeni lsyldakslc aaelvckewy  
181 rvtsgm1wk kliermvrt1 slwrglaerr gwqy1fknk ppgnappns fyralypkii  
241 qdietiesnw rcgrhslqri hcrsetskgv yclqyddqki vsgrldntik iwdkntleck  
301 riltghtgsv lclqydervi itgssdstvr vwdvntgeml ntlihhceav lhlrfnngmm  
361 vtcskdrsia vwdmasptdi tlrrvlvghr aavnvdfdd kyivsagdr tikvwnstc  
421 efvrtlnghk rgiac1qyrd rlvvsgssdn tirlwdiecg aclrvleghe elvrcirfdn  
481 krivsgaydg kikvwdlvaa ldprapagtl clrtlvhsg rvfrlqfdef qivssshddt  
541 iliwdflndp aaqaep1rsp srtytyisr

The yeast F-box protein Grr1p is encoded by a nucleic acid sequence corresponding to GenBank Accession No. M59247 (SEQ ID No. 5) as shown below, and which

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encodes the F-box protein corresponding to GenBank Accession No. AAA34652 (SEQ ID No.6)  
as shown below.

SEQ ID No. 5

1 cacgctaatac atgactcaaa taaatccata aagttttata cagtttttaa aaatatcatc  
61 atctattacc cagatgtgtt aatgaaccat tctatagtca tcattactag gctttcatta  
121 ctactgaggt taccgccta tggaccttcc ttggtaaagg aacttgtttt aaaatttgcc  
181 ttttaacaaa tttagtata tgattatcaa aaaaggcgtg gcaaaatata taacacccaaa  
241 ttttaactgtg cctgtgtgtt actttctttt gtccatactt caccagtttt tcgattttac  
301 acaataattc gttttcattt aatcgttctc ttagaagccc ggtttttgaa tatcaaaatc  
361 gtacttgtgt ccaactagca ggggaagccca aaaattaagg cattgcattt aagcttacac  
421 ctgctgaaa tcttgaaatt tctcattgat ttcggcacia taattatcat tggtagtgag  
481 gctaaacagt ttgctgtttc ctttatacta agaaggtcta taatggatca ggataacaac  
541 aaccacaatg acagcaatag gctgcaccca cctgatatac atccaaattt gggccctcaa  
601 ttgtggctga atagtagcgg tgattttgac gacaacaaca acaacaaca caacaacaac  
661 aataataata gcacaagacc acaaatgcca tcacgaacta gagaaacggc aacttcggaa  
721 agaaatgcaa gtgaggttag ggatgcaacg ctaaataata tctttaggtt cgatagtatt  
781 caacgggaaa cgcttttgcc aaccaacaac ggacaaccgc taaatcaaaa cttttcgtg  
841 acatttcaac cacaacagca acaaatgcg ctgaacggga ttgacataaa cactgtgaac  
901 acaaactta tgaatggtgt caatgttcaa atagatcaac ttaatcgatt gttaccgaac  
961 ctaccagagg aagaacggaa gcaaatccac gaattcaagc taatagtggg caaaaaaatc  
1021 caagagtttc tggttgttat agagaaacgt agaaaaaaaa tactgaacga aattgagcta  
1081 gacaacctta aactaaagga gctacgtatt gataactccc cacaagcaat tagttatttg  
1141 cataaattac aaagaatgag gcttagggcg ctagagacag aaaacatgga aattagaaat  
1201 ttaaggctaa aaatattaac aattatagaa gagtacaaaa agtcattata tgcatactgc  
1261 cattccaagc taagaggtca acaagtggaa aatccaacag ataatttcat catttgata  
1321 aactccatag atactactga atcatctgac ttgaaagaag ggctacaaga tctttcgaga  
1381 tattcaaggc agttcataaa taatgtggtt tcgaatccat caaatcaaaa catatgtacg  
1441 agtgtcacc gaagatcacc tgtgtttgac ctaaactatgc taccctcgga aatattacac  
1501 ttaatattag ataaacttaa ccaaaaatat gatattgtaa aattccttac cgtttccaaa  
1561 ctctgggctg aaataattgt gaagatactt tattacagac cgcacatcaa caaaaagagt  
1621 caattagact tgtttttaag gactatgaag ttaacttctg aagaaactgt attcaactat  
1681 cgtttaatga tcaaaagatt aaatttttca ttgtttggtg actacatgca cgatacagag  
1741 cttaactatt ttgtcggatg taagaatttg gagcgactaa ctttagtatt ttgcaagcat  
1801 ataaccagt ttccaatata ggctgttttg agaggtatga aatttctcca aagtgtggat  
1861 atcactggaa taagagacgt ttccgatgac gtatttgata ccttagcgac atattgtccc  
1921 agagtacagg gcttttatgt tccataggca aggaatgtaa cattcgattc actgcggaat  
1981 ttcatagtcc attccccgat gttgaaaaga ataaaaatca cagcaacaaa taacatgaat  
2041 gacgaattag tagaactatt agccaacaaa tgcctttgct ttgtagaggt cgatataaca  
2101 ttaagtccaa atgtcactga ttctagtttg ttaaaactcc tcaactaggt agttcagctg

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2161 agggaattca gaataactca taatacgaat attacggata atcttttcca ggagctttct  
2221 aaagtagttg acgatatgcc ctctttaaga ttgattgatc tttctggatg tgaaaatatt  
2281 acagataaaa ctatagaaaag tatagtcaat ttagccccta aattacgtaa tgtttttcta  
2341 ggcaagtgtg gccgaattac agatgcatcg ttgttccaat tatcgaagct gggcaaaaac  
2401 ttgcaaacag tgcatttttg gcaactgtttc aatataactg ataacggggt aagagcactc  
2461 tttcattcat gtacaagaat acagtatgtg gactttgcgt gctgtacgaa ttttaaccaat  
2521 agaactcttt atgaactagc agacttacca aaattaaaga gaattggcct tgtcaaagt  
2581 acgcaaatga ctgacgaggg tttgttgaat atggtttcct tgcgaggcgc aatgatact  
2641 ttagaaaggg tacattttatc ttactgttct aatttaacaa tatatccgat atatgagctt  
2701 ctaattgtct gcccaaggct ctacacattg tctttgactg ctgttcgcgc atttttacgc  
2761 cccgatataa cgatgtattg caggcctgca cctcagact ttagtgaaaa tcaacgtcaa  
2821 atattctggg tattttcagg gaaagggtt cataaacttc gccattattt agtaaattta  
2881 acgtcgcccg cttttggacc acatgtcgat gtaaatgatg ttttgacaaa atatattaga  
2941 tccaagaatt tgatatttaa cggtgaaaca cttgaagatg ctcttaggag aatcataact  
3001 gattttaaate aagattccgc tgcaattata gctgctacag gattaaatca aatcaacggg  
3061 ctaaataacg attttctttt ccagaatatc aattttgaac gaatagatga agtattcagt  
3121 tggatatctca atacttttga tggcattagg atgagctcgc aggaagttaa ctactatta  
3181 ttgcaagtaa acaagacgtt ttgtgaagat ccatttagtg atgtggacga tgatcaagat  
3241 tatgtcgtag cacctggtgt aaaccgggaa attaacagtg aaatgtgtca tattgttaga  
3301 aaattccatg agttaaatga tcatattgat gatttcgagg tgaatgttgc tagtttggtg  
3361 agagtccagt ttcagtttac tggtttttta cttcatgaaa tgactcaaac ctatatgcaa  
3421 atgattgaat taaacagaca aatttgttta gtacaaaaaa cggttcagga atcgggcaac  
3481 atagattacc aaaaagggtt tttaatatgg cgacttttat tcattgacaa attcattatg  
3541 gtggttcaga agtacaagct ctccaccgtt gttttgagac tatatttaaa agataacata  
3601 acattgttaa ccagacaaag agaactatta atagcccacc aaagatcagc atggaataac  
3661 aataatgaca atgacgcaa cgggaacgc aacaacatag tgaatattgt atcggatgct  
3721 ggggcaaacg atacaagtaa caatgaaact aacaatggta atgatgacaa tgaaacagaa  
3781 aatccaaatt tctggcgta gtttggaat agaattgcaa tatcacctga ccagatgagg  
3841 aatctccaaa tgggacttcg taatcagaac atgttttaga acaataacaa caacacaatt  
3901 gacgaatcaa tgcttgacac tgccattgat tctcaaatgg atgaagcatc aggaacgccc  
3961 gatgaagata tgttataatt gtatttcatt gaatacttac tgtctacta cacctttatt  
4021 ttcaaaatcc cacttttctt acttatttac atataaatc ataattgcatt cactttgaaa  
4081 ctttttgctt tagcatgtat acgctataga cttgcggtat caacgaatat acgtaacggt  
4141 gtcacgtcca cagaagatgc tatgtcaaca gttccctgca gatattctgcg atgcggcgaa  
4201 acattctata cacagtttca aaactacaaa aaatacaaac ctttagcctg tttatcaaat  
4261 tagttagcta taaaatgccc attttcttag caatatcgat caattgattg tcatcttcca  
4321 aagtttcaat aaaatttgtg gcagtatagt aatcccttct caatatgtcc aatttcttat  
4381 cacagtcac tataaattcg cgcttaatag attgcacttt taggttacc caattgttga  
4441 atgtcatgat ccaactcttc tgcaggattt

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1 mdqdnnnhnd snrlhppdih pnlgpqlwln ssgdfddnnn nnnnnnnnns trpqmpsrttr  
61 etatsernas evrdatlnni frfdsiqret llptnnggpl nqnfsltfqp qqqtналngi  
121 dihtvntnlm ngvqvqidql nrllpnlpee erkqihefkl ivgkkiqefl vviekrrkki  
181 lneleldnlk lkelridnsp qaisylhklq rmrlralete nmeirnlrlk iltiieeykk  
241 slyaychskl rgqqvenptd nfiiwinsid ttesdldkeg lqdlrsysrq finnvlsnps  
301 ngnictsvtr rspvfalnm1 pseilhlild klnqkydivk fltvsklwae iivkilyyrrp  
361 hinkksqldl flrtmkltse etvfnyrlmi krlnfsfvgd ymhdteinyf vgcknlerlt  
421 lvfckhltsv pisavlrgek flqsvditgi rdvsddvfdt latycprvqg fyvpqarnvt  
481 fdslrnfiyh spmlkrikit annnmndelv ellankcp11 vevditlspn vtdssllkl1  
541 trlvqlrefr ithntnitdn lfqelskvvd dmplslrldl sgcentdkt iesivnlapk  
601 lrvnflgkcs ritdaslfql sklgknlqtv hfghcfnitd ngvralfhsc triqyvdfac  
661 ctlnltnrtly eladlpklkr iglvkctqmt degllnmvsl rgrndtlerv hlsycsnlti  
721 ypiyellmsc palshls1ta vpsflrpdit mycrpapsdf senqrqifcv fsgkgvghklr  
781 hylvnltspa fgphvdvndv ltkyirsknl ifngetleda lrriitdlng dsaaiaaatg  
841 lnqinglnnd flfqninfer idevfwyln tfdgirmsse evnslllqvn ktfcddpfsd  
901 vdddqdyvva pgvnreinse mchivrkfhe lndhiddfev nvaslvrvqf qftgflhem  
961 tqtymqmiel nrqiclvqkt vqesgnidyq kglliwrl1f idkfimvvqk yklstvv1rl  
1021 ylkdnitllt rqrelliahq rsawnnnndn danrnanniv nivsdagand tsnnetnngn  
1081 ddnetenpnf wrqfgnrmqi spdqmrnlqm glrnqnmvrn nnnntidesm ptdaidsqmd  
1141 easgtpdedm 1

The yeast F-box protein Met30p is encoded by a nucleic acid sequence corresponding to nucleotides 3742 to 5664 of GenBank Accession Nos. Z46861 and Z47047 (SEQ ID No. 7) as shown below, and which encodes the F-box protein corresponding to GenBank Accession No. CAA86905 (SEQ ID No.8) as shown below.

SEQ ID No. 7

1 tttcttggtg cttcaacgga ttatcttaaa aaaatctatc atattttcaaa atataaatc  
61 ttattttttac aaagaagata tagattatgc ataataattat tttgtttacat tttttttctt  
121 ttactttttta ttttcttttc tttgtacttc ctcaaataag catcttttagc aggttaacaa  
181 tagcaaatat catgtccagc ccaaatacaca taatactttc cacttcaactt tcactatctg  
241 tttcgggaga cctatcatcc acggtattga cagtggtct tggaaatca gttgcatgtg  
301 cccaaggaat ggatctcgaa atgttctcaa acacggagga ccttcttctg aaagtccac  
361 ggtaagcggg cataggttcg gcaaaactgt gaggattatt gtcatgtgaa ggcgtgatag  
421 gtatgtcggt aagtgatgaa aaggcttttg aacccaaatc actactatcc atagaatcat  
481 caccgacctg cgcaattgga taaggcagag gagcgtcact ggtaaccctg aataggtgaa  
541 cattggcaac atgttcattt tcgactctga agatgatcca aacgaatctt cttaaaacct

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601 ccaaaagggc caatataaac gacgtcacag cactctgctg aattgtttga ggagcaattg  
661 cgtatacaat ccactcaaat ctaatgagga tatcccaa catagcaaag taataaacta  
721 acttctact gaatgaataa ctgccgtttt cccaattttt tttaccagct aaatacaagt  
781 cgtctcttag caaccaattg taagaagtag tattgtgagc aaaggaccaa tccataacta  
841 aatcccaggc ggaagtaagg atcgaattca acgtagcgca cacgataaaa ggggttctcc  
901 tttgttcaga acggtctgac aatctgtaag cacaaagtgt ggcattatac gctataacca  
961 aagtgtattt cgccgcgttc aaaagatgag ggaaccaatc accggaatca gcaaattctc  
1021 gtaaacattg catgaatctc caataacttg gtaaacatga taaaacaccc attgctctgg  
1081 aatgtgaaga gccacataga ttgttggcg tatgagagta aacacagaag aacatggcaa  
1141 tatcggaat agaatacgtc aacgaacaaa taatatctcc caaaaagaaa tcaccaaact  
1201 caacaggga aaaaccagac atcatcagtc taataagagt aaccaccagc cttttctag  
1261 tgtgtacaac tttgtccaa tatggaatta gaccagagg acataaaaat aagaaagaca  
1321 caataccaat atataaaaag cctaagggtg tgagcttctc caaagcgaaa cttaacatgg  
1381 aacagaccgc acaaggact atgaagaatg tcaagaaata caacttgagc ggaattttac  
1441 tcgtggcaaa atcattgtg aaaaattgag taccattctt ggattgaatc tcaccagca  
1501 taataaatct ataattaatc ccggttctat gccagataaa acaattaaca agaaagagaa  
1561 acgcgatcaa caaaaccatg taccaaccac cccacagtgg gaacagaatc ttgtgcgtaa  
1621 atgacgtttc ttcagagcta atgcccaaat acaaagtgt agtgatcaaa gtcattgaca  
1681 cacctatgcc cagcccgaca accagcatct gcacaatcga tctgtgtgtt ctatgaacca  
1741 tttgttcgga gatagagtag tgaatggtca atttcttcaa cttatgggta ttgtgcttcc  
1801 tgtccttagg cgaattggc aacgtagtgg tgaaccactc ggtgatctgc gtttccaacc  
1861 aagtgatggg ctctttgtct ctttggcg aagagagctc cgaagtgggt gttggttgcg  
1921 aactgggtat ttgttgcatc ttctgtgcca ccaactgcac gttggcatcc gcgtgcttga  
1981 aaagggtgta gtgggtcctg gcgtacgaca tgaacgtggc cagctctctt gtgtgacacg  
2041 ttttgtcgaa tttcttgacc attttacgga acccggtgac gttgatatcc cggaacgatt  
2101 tgaccaattg caagtacaga tagtactcga ttatagcgtt gcttaacaag tttctagcct  
2161 gggttgtcgt catagtctcc agaaaagaag cgcctaaaagc aaacgtctcg cggcctcttg  
2221 aggacgcac ctgtctcaag tcctgtagca gagaaaatcc acgtttgggc cacgatggca  
2281 gcagcctatt gtccttaaga actttctgac agtacgtag cagcgacaaa cgcggcttct  
2341 tggcctctt ggtgcaggc attgacccat acataacaga cggctatcg ctgtcgatgc  
2401 tattgaccct ggagtcagaa cgaccagcaa gccctgcgc atatagactc gtggacatgt  
2461 caacattcga actagaccgg ttcaagttgt cgcgctcata attcttctgc agcgagtaat  
2521 agtgcagttg cgactgtaa acctcaact tcttgtcga ctcttttagc aaccaaaggt  
2581 aaaactcgtt acacttactc aactggaacg agatcaacca gtcttcaatg aagtcagcaa  
2641 cgaactccct ctgcaaagca gaatagtctt tcttgaacgc aggtccggag cgatagtctc  
2701 cgtcgctgcg acttttgccg ggctctctct gctgaaatgc agtctggtat accgacacag  
2761 agggcatcca gctccggtag gagctggatt gctcttcttc ggcattcagc ttctcttgt  
2821 agcggcgaag cttcttcttg ccgacctat aatcaatata tttgtccctc cattccggga  
2881 tggcagactc ggtagatgg tcagcaaaact tcatctgata cgggtgtatg gtaaagccct  
2941 tccattgctg ccaactgaat taaaaaaaaa aaaaaataa ctaccaacca tcaaatcaaa

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3001 caaaacaaaa caaaaaagca aaggagaaaa cccatcttgt acatgtacag tcccaaactg  
3061 ttgcgaaacc gtgcgatgat gttcatggaa cttgcgtcaa ataaaaccgc atcccgcccc  
3121 acgtgacaaa cggcacccaa aatccgttct agaaatgcct cacaccacac ccgatgatgg  
3181 gcttcgact cgatgactac caacacatag ccagccgcag cggctggcag catgtgcatg  
3241 ataataataa gtgatgatga atgatgggtga taacgatttt gaacaaatgg ctgcagcgat  
3301 agcaactaag gggatggaaa gacagatctg ggagagataa ctgcagggtg tggcacggca  
3361 acacaaggct attgtattgc actaaacggg caagaagcca tgatgtgcgt ctgtatccca  
3421 aaaaaaaaaa taatggattg gcgcgtgtac tatatatatt catatgtcgt gtgtttgtat  
3481 atgtgtggga gtgattgtgc gtgtatatgt gtgttggcgt gtgtggtaca atgtgtgtgt  
3541 tttaatgtag aatgaggtt gtagcacgtg atcgggaagc cacagtttgc gcggagatat  
3601 tttatTTTTT ttcacagcg taagaagaaa gcaaccttgc agtctgtatc gtaagagaag  
3661 actgcagtta aagaagtta gagaagaggc ttgagtatcg gtaaaggggt gtgtgtttgg  
3721 tgatttataa aggagaagg catgaggaga gagaggcaaa ggatgatgag tttcgaggac  
3781 aaggacaagg acgacttga caatagtaat agtaataaca gcagtgaat gacagatagc  
3841 gcgatgatgc caccattaaa gagattgctt attacgggca gtagcgatga tttggcacia  
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3961 ttggcgacaa acgacagcgg cactagggtg cagccattgc cagaatataa cttcaccaag  
4021 ttctgctatc ggcataaccc ggacattcag ttctcaccaa ctcatacagc gtgctacaag  
4081 caggatttga aacgaacgca agagattaat gctaatatcg cgaagctacc cctgcaggag  
4141 caatccgaca tccaccacat tatctcgaag tacagcaatt ccaatgacaa gatacggag  
4201 ctgattctgg atgggatcct atcgacgagt tgcttccac agctttccta catttcgtca  
4261 ctgcttacac acatgatcaa gatcgacttc atcagcattc tgccgcagga gctgtcgtg  
4321 aagatcttga gttatctgga ttgccaatct ctttgcaacg ccacgagagt gtgccgcaag  
4381 tggcagaagc tcgcggatga cgacagggtg tggtagcaca tgtgagagca gcacatagac  
4441 aggaaatgtc ccaactgtgg ctgggggctg cctcttttgc acatgaaacg tgcgcggata  
4501 caacagaata gtacaggatc tagcagcaac gcagatatcc agacgcaaac tacgcgacct  
4561 tggaaagtca tctacagaga acggttcaaa gtggagtcaa actggagaaa gggccactgc  
4621 aggattcagg aattcaagg ccacatggat ggtgtgttaa cgtccagtt taactacagg  
4681 cttttgttca caggctcgtg cgactccacc ataggtatat gggacttatt cacggggaag  
4741 ctaatacgaa ggctcagcgg ccattcggac ggcgtcaaga cattatatatt tgacgataga  
4801 aagctgatta cgggctcgtc cgacaagacg atcgtgtttt ggaactacat aaccggtgaa  
4861 tgcatttcca cgtatcgagg ccactcggat agcgttctga gcgtagattc ataccagaag  
4921 gttatcgttt ccggcagtgc tgacaagacg gtcaaggat ggcacgtgga gtccaggaca  
4981 tgctacacct tgagaggcca cacggaatgg gttaatgtcg tcaaattgca tccgaaaagc  
5041 ttttcatgtt ttagttgcag tgacgatacc acaatcgaa tgtgggatat caggaccaat  
5101 tcatgcctaa aagtgttcag gggatcatga gggcagggtc aaaagatcat accgcttacc  
5161 attaaggatg tagagaatct agccaccgac aacattctg atggcagctc tccgcaggat  
5221 gaccaacaaa tgactgatgg tgcagacgaa tcagacacac cgtcgaaacg gcaagaaact  
5281 gtcttagatg aaacatacc ttatccaaca catctactat cttgcggact ggataacaca  
5341 atcaaaactat gggacgtcaa aaccggtaaa tgcataagaa cacagtttgg gcacgtggaa

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5401 ggtgttttggg acatcgccgc tgacaacttc agaattataa gtgggttctca cgacggaagc  
5461 attaaggtct gggacttgca aagcggggaag tgtatgcaca cgttcaacgg tcgaagacta  
5521 caaagagaaa ctcagcacac acaaacacaa tccttgggtg ataaagtcgc ccctatcgct  
5581 tgtgttttgta ttggagattc agaatgcttt agtggtgatg aatttgggtg cgtaaaaatg  
5641 tacaaattcg atctcaatga ttaggacctg tgtgtggtct tttcttggtc aaaaacatcc  
5701 gtagtacctc gaatatatat gcttacatat ataataaaaa atacataata gcattttaca  
5761 tttattttat ttccaggaaa aaaataaatc gctagcgtat cactagcctt ttccatcttc  
5821 agtttttttc cttcctcttt ttcgtctcga taaaactctt gaccattaga tgctattact  
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 22621 ctgccgttat tatttcgttt agttactaca tttatgggtat aaattacctt taagacatta  
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24601 tctggtcagt tcttggtttg tccaagtgca gaatgattgt agtgggtgact ctatagttga  
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 25561 taaacgttga aaaccacttt tccccaatgt ggcaactttg gttctctttg tagcagtcac  
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 25741 ataaaagttc tccccttgat caccctcgcg aatgattgtt tcaccgggt ggtagatctt  
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 26581 aacaatgttc tttgccttaa attcaggctc cctggccttg aggaacgctc tctgttggtc  
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 26701 gatttcgttc tggaacagtt gcaattcggc ttgcgattcc ttggggcaag aagataccat  
 26761 cgtttattct tactgttgct ttttgaaaat aatctgcttg ttgtaaata tcttctatt  
 26821 tatgtatgcg tgaaatgcgt gtaatggatg tgatgatagc gatcgcttga cttagtcgag  
 26881 gaaagcgtaa agtgtccctt tttctcttcc ccttttccct gtttgttcaa attttctctt  
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 28021 caaagctctc ctttgaaaag acactcatca ctcaaaagca cttccaatgg tcttttggtc  
 28081 caaatgtcta ataattctggg gaattggttca ccggaaccgg cagtagcgag cacttctcca  
 28141 aatggctcaa ttatttccac taaactaaat ttgaacggcc aattttcttg cgttgattcg  
 28201 aaaacattgc gaatttatcg gcataaagca ccatgcataa tgacttttgt ctcagatcat  
 28261 aatcatccga aattttcatt gtattttcaa caatcgggtga tctacaattc acaagttaat  
 28321 ctgcttgatg atgttgaatt gataatttta gataagaaga actcttttat ggctataatt  
 28381 ttaaaagatc tgaaaaaggt caagatgata ctgacgtga ataactcttc aatcaacatt  
 28441 aacacgaaca tcttgatatg gtccactgca agctccgctt caaataaaaa aataaagtct  
 28501 attaaaagat tctgttgat gtcataattc tcgtcgataa aagtcgaaat tttagatcat  
 28561 aaagagcaga ttttggaag actaaaacat ctgattcatc ctatttcttc gtcatcacct  
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 28741 tcaaacaaac ctcatgggtt gcaatcctta acaaaaagga ctcgatttgc cagccttggg  
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 29281 aagtacgttg ttataccaat taacataagt tatcattggt ttagttgcat tataacaaac  
 29341 ttggatgcga tcttggtttt tcatcaaaac aaagataaaa acgatgccat caactccgat

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cmf*

[illegible]

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61 mtmatrspss spdlatndsg trvqplpeyn ftkfcyrhnp diqfspthta cykqdlkrtq
121 einaniaklp lqeqsdihih iskysnsndk irklildgil stscfpqlsy isslvthmik
181 idfisilpqe lslkilayld cqslcnatr crkwqkladd drvwyhmceq hidrkcpcncg
241 wglpllhmk ariqqnstgs ssnadiqtqt trpwkviyre rfkvesnwrk ghcriqefkg
301 hmdgvltlqf nyrlfftgsy dstigiwdlf tgklirrlsg hsdgvktlyf ddrklitgsl
361 dktirvwnyi tgecistyr hsdsvlsvds yqkvivsgsa dktvkvwhe srtcytlrgh
421 tewvncvklh pksfscfscs ddtfirmwdi rtnsclkvfr ghvgqvqkii pltikdvenl
481 atdntsdgss pqddptmtog adesdtpsne qetvldenip ypthllscgl dntiklwdvk
541 tgkcirtqfg hvegvdiaa dnfriisgsh dgsikvwdlq sgkcmhtfng rrlqretqht
601 qtqslgdkva piacvcigds ecfsgdefgc vkmykfdlnd

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The fission yeast F-box protein Pop2 encodes a novel F-box/WD-repeat protein involved in the proteolysis of the Cdc2p inhibitor Rum1p and the replication initiator Cdc18p and is encoded by a nucleic acid sequence corresponding to GenBank Accession No. AF038867 (SEQ ID No. 9) as shown below, and which encodes the F-box protein corresponding to GenBank Accession No. AAB95480 (SEQ ID No.10) as shown below.

SEQ ID No.9

1	atgtcactct	ctaggtgtcc	aactgacaat	tcgctcctcc	gtataaattc	ctctgttctc
61	ttaataaata	gcagcagccc	tgctacacct	ccagaatcat	ttgatcctca	agtatttctc
121	tcttcactta	ttcatgggga	taacctgctt	cctcaagatg	atcaaattgc	atcggatcct
181	cgctcagaat	caaatagttg	taatggcaat	acgagttctt	ccctgccgtg	cactgattcg
241	tatcagtacc	cattaaagca	ttcttgtacg	ccttcttttc	ttcgaaagt	taatgaaagt
301	atagagaatg	tctcttataa	atgcttagac	cactcaccgc	cagatagtgt	tcctggcgat
361	ttttccattt	cccttggtcc	tcaaaggaa	tttctatatt	ctcattcttc	tcttccacct
421	aaaattatat	caattgatag	aaacaatcga	attaagttag	ataatagcat	ttcatctaac
481	tccgacaatt	tccctccttc	tccgaaagtc	gacacatcaa	acactgtttc	acctggtagt
541	aaacctatct	ctgaggatct	tgaagattta	aacttacagt	caattgttca	aacttttgag
601	gatcttccag	aaggaattca	atcttatgcg	ttttttcaac	tactccgttc	gtgcaatcgg
661	caatcgatgc	gtttattatt	gaatgaatgc	gagccgcttc	taaaaaaga	tatactttca
721	aatcttctct	tttccattgt	tcagctctata	ttattaaatc	tggatataca	ttcttttctt
781	tcttgccgtc	ttgtttcgcc	tacttggaat	agaatacttg	atgtgcatac	ttcatactgg
841	aaacacatgt	ttagtttatt	tggctttcaa	atcaatgaaa	atgactggaa	atatgctaat
901	ccaaacttaa	atcgctccacc	ttttttgcac	aacgaccaa	tctcagatga	ctattttccg
961	gaaattttca	aaagacattt	tctcaataga	aaacgatgg	tatttccttc	gatacctcca
1021	agtcatctat	cttttcccat	tcatgttcca	aactttatga	taacttcttt	actacttcat
1081	aaagacagaa	taatcaccac	ttcgggatct	ggaacaattc	aaattcataa	tgctattacc
1141	ggtgttttag	aagctcgatt	agagggctcat	aaagaagggtg	tttgggctgt	caaaatacat

1201 gagaatacac ttgtatctgg ttcatcgat aaaactgttc gcgtttggaa catagagaaa  
 1261 gctaaatgta cgcacatatt taggggacat atttccatca tcagatgctt agagatctta  
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 1381 gtcagcggct ctgggatca tacacttcgg gtttgggaagc ttccaaaaaa cacggatcct  
 1441 ccttatcttc cagataatac aaactctatt gaccgttggg agaagaacct gtattttgta  
 1501 catactttga taggacatac agactctgta cgaactatat ccggctatgg tgatatactt  
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 1801 aggttgatat caggttctgc tgactccaca attagaatat gggatttgaa tactgggaaa  
 1861 ccattaatgg ttttgccgtc taattcaggc tacattagta gctttgtgtc agatgaacac  
 1921 aaaattatta gtggaatga tggttctgta aagttatggg atgttaggac tggaaagctg  
 1981 ttacgttttc tattaacaga cctcacaaaa atatggcatg tcgattttga tgctatgcgt  
 2041 tgtgtggctg cagtgcagcg tgatgatcaa gcatatttgg aagttattaa tttttccgga  
 2101 tcaagaccgt ag

#### SEQ ID No.10

1 mslsrcptdn sssrinssvp linssspatp pesfdpqvfp sslihgdnl1 pqddqiasdp  
 61 rsesnscngn tssslpctds yqyplkhsct psflrkfnes ienvsykcld hspdpvpgd  
 121 fsislvpqrn flyshsslpp kiisidrnrr ikldnsissn sdnfppspkv dtsntvspgs  
 181 kpisedledl nlqsiqtfe dlpegiqsyf ffqlrscnr qsmrlllnec epllkdkdils  
 241 nlpfsivqsi llnlidhsfl sclvsptwn rildvhtsyw khmfsllfgfq inendwkyan  
 301 pnlrppflh ndqisddyfp eifkrhflnr krwlfpispp shlsfpihvp nfmitlslh  
 361 kdriittsgs gtiqihnait gvlearlegh kegvwavkih entlvsgsid ktvrwniek  
 421 akcthifrgh isiircleil vpsrlirhgv eivepdqpyi vsgsrhdhtr vwklpkntdp  
 481 pylpdntnsi drweknpyfv htlightdsv rtisgygdil vsgsydssir iwrvtstgecl  
 541 yhlrghslri ysvlyepern icisgsmaks irvwdlstgt ckyvleghda fvtllnvfq  
 601 rlisgsadst iriwdlntgk plmvlpnsng yissfvsdeh kiisgndgsv klwdvrtgkl  
 661 lrflitdltk iwhvdfdamr cvaavgrddq aylevinfsq srp

The murine F-box protein FWD1p involved in ubiquitin-dependent degradation of IkappaBalpha and is encoded by a nucleic acid sequence corresponding to GenBank Accession No. AF081887 (SEQ ID No. 11) as shown below, and which encodes the F-box protein corresponding to GenBank Accession No. AAD17755 (SEQ ID No.12) as shown below.

#### SEQ ID No. 11

1 gaattcggca cgaggcggag ctgcgttggc tgccgcctgg cacgaaaggg gcggccccgg  
 61 cggagagcag acccagtagt cccggcgatc atggaccggc cagaggcggt gctgcaggag

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A1  
cont



